REMARKS/ARGUMENTS

Claims 1-73 are currently pending. Claims 1-12 and 27-73 were withdrawn pursuant to a restriction requirement mailed March 21, 2006. This Amendment cancels claims 1-12, 17, and 27-73, adds new claim 74, and amends claims 13-15, 18-20, and 22-26. The paragraph numbering below follows that of the Office Action.

New Claim

Support for new claim 74 can be found in the specification at, for example, page 9, line 30 to page 10, line 6. No new matter is added.

¶6. The first sentence of the instant specification is amended to indicate that USSN 09/469,655 is now patented.

¶7. The title of the invention is amended and is indicative of the subject matter to which the presently pending claims are directed.

¶8. The paragraph beginning at page 27, line 5 is amended to delete "ELIZA" and insert therefor "ELISA".

¶9. The heading "Agents that bind [...]" on the Abstract page (page 37) is deleted.

¶11. First Rejection Under 35 U.S.C. §112

Claims 13-26 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. This rejection is traversed.

¶11A. Claims 13, 16, 23, and 24 are allegedly indefinite in the recitation of "MAb 763-15-5" and "MAb 292-2-3." Amended claims 13, 23, and 24 recite "MAb 763-15-5 (ATCC PTA-1079)", and amended claim 16 recites "MAb 292-2-3 (ATCC HB-12645)." Withdrawal of this rejection is respectfully requested.

¶11B. Claim 13 is allegedly indefinite in the recitation of "2C-catalyzed metabolism." Amended claim 13 recites "2C9*1, 2C9*2, and 2C9*3 catalyzed metabolism." Withdrawal of this rejection is respectfully requested.

¶11C. Claims 15, 25, and 26 are allegedly indefinite in the recitation of "the enzyme activity." Amended claims 15, 25, and 26 recite "the phenanthrene metabolism enzyme activity." Withdrawal of this rejection is respectfully requested.

¶11D. Claim 16 is allegedly indefinite in the recitation of "binding fragment thereof." Amended claim 16 recites "a binding fragment thereof that binds to 2C9*2." Withdrawal of this rejection is respectfully requested.

¶11E. Claims 18-20, 23, and 24 are allegedly indefinite in the recitation of "the monoclonal antibody." Amended claims 18-20, 23, and 24 refer to amended claim 13, which recites "a monoclonal antibody." Withdrawal of this rejection is respectfully requested.

¶11F. Claim 22 is allegedly indefinite in the recitation of "prokaryotic cell line." Amended claim 22 refers to claim 20. Withdrawal of this rejection is respectfully requested.

¶13. Second Rejection Under 35 U.S.C. §112

Claims 13-26 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. This rejection is traversed.

¶13A. Claims 13-15, 25, and 26 allegedly lack enablement due to the recitation of "binding agent." Amended claims 13-15, 25, and 26 recite a "monoclonal antibody." Withdrawal of this rejection is respectfully requested.

¶13B. Claims 13-26 allegedly lack enablement for binding under all conditions. Amended claim 13 indicates binding between the monoclonal antibody and the human cytochrome p450 2C9 allelic variants 2C9*1, 2C9*2, and 2C9*3 is detectable by an enzyme-linked immunosorbent assay. Presently pending claims 14-16 and 18-26 depend directly

or indirectly from amended claim 13, and therefore are enabled as depending from an enabled base claim. Withdrawal of this rejection is respectfully requested.

¶13C. Claim 16 allegedly lacks enablement for competitive binding between MAb 292-2-3 and MAb 763-15-5 for all 2C9 allelic variants. Amended claim 16 recites specific binding "to human cytochrome p450 2C9 allelic variant 2C9*2." Withdrawal of this rejection is respectfully requested.

¶13D. Claim 24 allegedly lacks enablement for light/heavy chain variable domains that include any three CDR regions. Amended claim 24 recites a light chain variable domain that includes "the three CDR regions" from the light chain of monoclonal antibody MAb 763-15-5, and a heavy chain variable domain that includes "the three CDR regions" from the heavy chain of monoclonal antibody MAb 763-15-5. Withdrawal of this rejection is respectfully requested.

¶13E. Claim 23 allegedly lacks enablement for a monoclonal antibody that is 80% identical to MAb 763-15-5 which retains the biological activities put forth in claim 13. Applicants disagree.

According to the Office Action, minor changes in CDR amino acid sequences can alter biological function. However, it is respectfully noted that the claimed monoclonal antibody of amended claim 23 retains the biological activities put forth in amended claim 13. Particularly, the monoclonal antibody competes with monoclonal antibody MAb 763-15-5 (ATCC PTA-1079) for specific binding to the human cytochrome p450 2C9 allelic variants 2C9*1, 2C9*2, and 2C9*3, and specifically inhibits 2C9*1, 2C9*2, and 2C9*3 catalyzed metabolism of phenanthrene by at least 50%. As further discussed below under **¶14**, the claimed monoclonal antibody of amended claim 23 can be defined by reference to its binding epitope, as determined by a competition assay. Such competition assays are well described in the specification.

According to MPEP 2164.01, the test for enablement is whether the specification contains sufficient information regarding the subject matter of the claims as to enable the artisan to make and use the claimed invention. The disclosure of the claimed antibody with regard to

epitope specificity, along with a description of assays that can be used to determine competitive inhibition, provide such information so as to enable the presently claimed subject matter.

In fact, the instant specification provides considerable direction and guidance on how to practice the claimed invention. The specification discusses antibody production at, for example, page 13, line 21 to page 14, line 23. Sequence identity analysis is described at page 7, line 27 to page 8, line 10. Sequence analog screening is discussed in the specification at page 17, lines 1-16. The specification describes an antibody that binds to the human cytochrome p450 2C9 allelic variants 2C9*1, 2C9*2, and 2C9*3 that are also bound by MAb 763-15-5 (ATCC PTA-1079). Competition assays are discussed in the specification at, for example, page 11, lines 16-30. The level of skill in the art at the time the application was filed was sufficiently high such that that undue experimentation would not be required to practice the presently claimed invention. Thus, presently pending claim 23 is enabled. Withdrawal of this rejection is respectfully requested.

¶14. Third Rejection Under 35 U.S.C. §112

Claims 13-15 and 17-26 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking written description in the specification. According to the Office Action, the instant specification discloses just a single species of binding agent that can compete with MAb 763-15-5 for binding to the human cytochrome p450 2C9 allelic variants 2C9*1, 2C9*2, and 2C9*3, and that can specifically inhibit 2C9*1, 2C9*2, and 2C9*3 catalyzed metabolism of phenanthrene by at least 50%: MAb 763-15-5 itself. Applicants disagree.

According to MPEP 2163 II.A.3a, possession can be shown in many ways. For example, an adequate written description can be shown by a description of sufficient, relevant, identifying characteristics so long as an artisan would recognize that the inventor had possession of the claimed invention. This section of the MPEP also specifies that for some biomolecules, including antibodies, examples of identifying characteristics include binding properties.

A genus of antibodies can be defined under the written description guidelines by reference to its binding epitope. As noted above, for some biomolecules, including antibodies, examples of identifying characteristics include binding affinity and binding specificity.

Applicants submit that given an antibody, a binding epitope can be defined by a competition assay involving the antibody.

As described in the instant specification at, for example, page 11, lines 16-30, and at page 14, lines 19-22, competition can be determined by an assay in which the antibody under test inhibits specific binding of a reference antibody to an antigenic determinant on human cytochrome P450 2C family members, and antibodies can be selected to have the same epitope specificity as a particular MAb such as MAb 763-15-5.

Accordingly, the presently claimed genus can be defined by reference to its binding epitope, and possession of the MAb 763-15-5 antibody allows the binding epitope to be defined by a competition assay. Withdrawal of this rejection is respectfully requested.

¶16. Rejection Under 35 U.S.C. §102

Claims 13-15 and 25 were rejected under 35 U.S.C. §102(a) as allegedly anticipated by Tang et al., "Roles of human hepatic cytochrome P450s 2C9 and 3A4 in the metabolic activation of diclofenac," Chem. Res. Toxicol. 12(2):192-9 (1999) ["Tang"]. This rejection is traversed.

According to MPEP §2131, to anticipate a claim, a cited reference must teach each and every element of the claim. Tang fails to meet this test.

Amended independent claim 13 is drawn to a monoclonal antibody. In contrast, the Office Action notes that the anti-P450 2C9 antibody described by Tang is polyclonal. Thus, Tang is not an anticipatory reference. Presently pending claims 14, 15, and 25 depend from independent claim 13, and are therefore allowable as depending from an allowable base claim, as well as for the novel combination of elements they recite. Withdrawal of this rejection is respectfully requested.

¶18. Rejection Under 35 U.S.C. §103

Claims 13-15, 17-21, and 25 were rejected under 35 U.S.C. §103(a) as allegedly obvious over Mei et al., "Role of a potent inhibitory monoclonal antibody to cytochrome P-450 3A4 in assessment of human drug metabolism," J. Pharmacol. Exp. Ther. 291(2):749-59 (1999) ["Mei"] in view of Tang and U.S. Patent No. 6,242,203 to Melvin et al. ["Melvin"].

According to MPEP §2143, a *prima facie* case of obviousness requires, among other things, that there be some suggestion or motivation to combine the references, and that the references when combined teach or suggest all the claim elements. The combination of Mei, Tang, and Melvin do not meet this test.

Amended independent claim 13 is drawn to a monoclonal antibody that competes with a monoclonal antibody MAb 763-15-5 (ATCC PTA-1079) for specific binding to the human cytochrome p450 2C9 allelic variants 2C9*1, 2C9*2, and 2C9*3, and that specifically inhibits 2C9*1, 2C9*2, and 2C9*3catalyzed metabolism of phenanthrene by at least 50%.

Mei reports that inhibitory monoclonal antibodies can be used to study cytochrome P450 enzymes. Tang reports a polyclonal anti-P450 2C9 antibody. Melvin discusses an antibody that reacts with cytochrome P450 form CYP1B1.

Mei focuses on the advantages of monoclonal antibodies. In contrast, Tang describes a polyclonal antibody. Thus, there is no motivation to combine Mei and Tang. Moreover, neither Mei, Tang, nor Melvin describe specific binding to the human cytochrome p450 2C9 allelic variants 2C9*1, 2C9*2, and 2C9*3.

Although Tang discusses a polyclonal anti-P450 2C9 antibody, to conclude that Tang's antibody inherently binds to allelic variants 2C9*1, 2C9*2, and 2C9*3 would be antithetical to the statements made in the Office Action at page 2, where the Examiner alleged that two different antibodies (763-15-5 and 763-15-20) both bind 2C9 yet reflect patentably distinct restriction groups. What is more, according to MPEP § 2112 (IV), that a certain result or characteristic ***may*** occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. To establish inherency, the extrinsic evidence ***must*** make clear that the missing descriptive matter is ***necessarily present*** in the thing described in the reference. In relying upon the theory of inherency, the Examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the cited reference.

Thus the combination of these references fail to teach all elements of the presently pending claim. Accordingly, the combination of Mei, Tang, and Melvin does not meet the

requirements for a *prima facie* case of obviousness. Withdrawal of this rejection is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-571-4000.

Respectfully submitted,

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